It is proposed that claims 23 and 68 each be amended to clarify this step by specifically reciting the phrase "determining the glucose concentration in the body fluid". Specifically, claims 23 and 68 are each amended to recite the step of "determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals". Support for the amendment is found in the specification at page 2 last paragraph to page 3 first paragraph and page 10 lines 12-21.

The rejection also proffers that there may be some confusion between the terms "content" and "concentration" in the claims. It is submitted that one of ordinary skill in the art is fully aware of the common meaning of each term and specifically that "content" is the amount of the specified substance and that "concentration" is the amount of the specified substance in a unit amount of another substance. Antecedent support is provided for each of the terms. Therefore, it is submitted that confusion does not exist as to these terms in the claims.

Regarding claim 68, the rejection proffers that the phrase "in alternating successive transport and dialysis intervals" is not understood. It is proposed to remove that phrase from claim 68.

The rejection further proffers that "measuring measurement signals" is unclear because no measurement signals have been obtained and what they might be measured for is not seen. It is proposed that claims 23 and 68 be amended to recite the step of "obtaining measurement signals that correlate with a glucose content of the dialysate in the measuring cell". Support for the amendment is found in the specification at page 8 lines 10-18 and page 10 lines 18-21. Accordingly, the claim now recites a step of obtaining measurement signals and specifies for what the signals are measured.

The rejection also asks the question as to how can one adjust the starting content of glucose if one must first measure the glucose concentration. It is submitted that one of ordinary skill in the art would readily recognize that a difference exists between perfusate and body fluid. With this in mind, the Examiner's attention is directed to the specific wording of the adjusting step of claims 23 and 68. That step does not adjust the starting of glucose generally, but rather adjusts the glucose content in the perfusate to the glucose content of the body fluid. Perfusate is not the same

thing as body fluid. Accordingly, if one is to adjust the perfusate's glucose content to the body fluid's glucose content, one must by definition determine what the body fluid's glucose content is. In order to determine the glucose content of the body fluid, one measures the glucose concentration in the body fluid.

The rejection further asks the question as to how the momentary starting content of glucose can be a measure of glucose content of the body fluid. Claims 23 and 68 each recite the step of determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals. This step is believed to be sufficiently definite for purposes of 35 U.S.C. 112, second paragraph. Moreover, this step is fully described in the specification. Specifically, the Examiner's attention is directed to page 2 paragraph 4 to page 3 paragraph 3, page page 5 paragraphs 1-2, page 10 paragraphs 2-3, page 11 paragraphs 3 and 4, and page 13 paragraph 2.

The rejection also states that "if a feedback is intended to adjust the starting glucose concentration, it is not found in the claims as presented." That rejection is respectfully traversed. It is submitted that feedback is found within the adjusting steps of claims 23 and 68 to adjust the starting content of glucose in the perfusate. Specifically, feedback may be explained as follows:

1. The perfusate has a starting content of glucose

2. Measurement signals are obtained that correlate with the glucose content of the dialysate (note: one of ordinary skill in the art would readily recognize that the perfusate is entering and the dialysate is leaving the microdialysis probe).

3. The starting content of glucose in the perfusate is adjusted to a value that corresponds to that of the body fluid, which value was derived from the measurement signals - which correlate with the glucose content of the dialysate.

Claim 76 as well as claims 48 and 49 has been amended to provide proper antecedent basis of the values presented. Moreover, claims 71-75, 77-79 have been amended to correct the lack of antecedent basis in the claims.

Claims 24-50 depend from amended claim 23 and claims 69-79 depend from amended claim 68. Accordingly, the claims are believed to be sufficiently definite for purposes of 25 USC 112, second paragraph and reconsideration of the rejection leading to its withdraw and allowance of the claims is respectfully requested.

The rejection under 35 U.S.C. 103(a) over U.S. Patent No. 6,091,976 to Pfeiffer et al. was maintained. The rejection proffers that the "adjusting step" of the claimed invention is so vague as to not be possible to distinguish from Pfeiffer. Moreover, the rejection proffers that the function of the teaching of Pfeiffer and that presently claimed invention appears identical. Those proffers are respectfully traversed. Unlike Pfeiffer, the idea behind the invention is to adapt the glucose content of the perfusate to the glucose concentration of the body fluid.

The adjusting step of claims 23 and 68 specifically recite, "adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid". This adjustment offsets glucose gradients and hence reduces the period required for a complete dialysis equilibration. The rejection incorrectly states that Pfeifer et al. sets the predetermined concentration depending on the tissue glucose concentration. A careful reading of Pfeifer et al. rather indicates that this concentration is set within the physiological range, for instance at 5 mmol/ltr. See, Column 4 lines 52-54. There is simply no disclosure or suggestion in Pfeifer et al. of adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid, as presently claimed.

At most, Pfeiffer conducts signal validation or qualitative comparison measurements by adjusting the starting concentration of glucose in the perfusate. See, Column 5 lines 10-13. These measurements, however, teach away from the presently claimed invention. Specifically, during these validity tests, the glucose concentration in the perfusion solution 30 may be alternatively adjusted to a sugar-deficiency value and to an excess sugar value to emit a warning signal. See, Column 5 lines 13-16. Accordingly, the only adjustment that is taught by Pfeiffer is to sugar deficiency and excess values.

In order to support an obviousness rejection, it is necessary that Pfeiffer et al. provide some teaching, suggestion, or incentive to be modified as proffered by the rejection. Here, it is submitted that only with hindsight, in view of Applicants specification, could one of skill in the art derive from Pfeiffer et al. a suggestion to the invention as it is presently claimed.

It is therefore respectfully submitted that Pfeiffer et al. cannot be said to provide suggestion or motivation to be modified to meet the requirements of amended claim 23, that being a method for continuously determining the glucose concentration in a body fluid with glucose-containing perfusate, wherein the method comprises the

steps of "providing a microdialysis probe, a measurement cell, and a control device, inserting the microdialysis probe into the body fluid, passing the perfusate having a starting content of glucose through the microdialysis probe to obtain a dialysate, transporting the dialysate to the measuring cell, obtaining measurement signals that correlate with a glucose content of the dialysate in the measuring cell, measuring the measurement signals that correlate with the glucose content of the dialysate, adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals." Claims 24-50 depend from amended claim 23.

Likewise, it is submitted that Pfeiffer et al. cannot be said to provide suggestion or motivation to be modified to meet the requirements of amended claim 68, that being a method for continuously determining a glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of "providing a microdialysis probe, a measurement cell, and a control device, inserting the microdialysis probe into the body fluid, passing the perfusate having a starting content of glucose through the microdialysis probe at different flow rates to obtain a dialysate, transporting the dialysate to the measuring cell, obtaining measurement signals that correlate with the glucose content of the dialysate in the measuring cell, measuring the measurement signals that correlate with the glucose content of the dialysate, adjusting the starting content of glucose in the perfusate to a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals". Claims 69-76 depend from claim 68.

It is respectfully contended that the differences between the claimed invention and the cited art are such that Applicants' invention as a whole would not have been

obvious to one of ordinary skill in the art at the time the invention was made. It is respectfully contended that the claimed invention meets the test of patentability under 35 U.S.C. 103(a). Entry of the amendments leading to reconsideration of the rejection of the claims and withdrawal of the rejection is respectfully requested.

This application is deemed to be in condition for allowance and as such is respectfully requested. In addition, it is requested that if necessary, that this paper be considered as a Petition for an Extension of Time sufficient to effect a timely response and fees be charged to Deposit Account No. 50-0877.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

23. (Twice Amended) A method for continuously determining [the] a glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of:

providing a microdialysis probe, a measurement cell, and a control device,

inserting the microdialysis probe into the body fluid,

passing the perfusate having a starting content of glucose through the microdialysis probe to obtain a dialysate,

transporting the dialysate to the measuring cell,

obtaining measurement signals that correlate with a glucose content of the dialysate in the measuring cell,

measuring the measurement signals that correlate with the glucose content of the dialysate,

adjusting the starting content of glucose in the perfusate to [the] a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and

determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals.

48. (Amended) The method of claim 33 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1-b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes [the] a peak value of the measurement signal and S_0 denotes [the] a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of

glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

49. (Amended) The method of claim 38 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1-b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes [the] a peak value of the measurement signal and S_0 denotes [the] a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

50. (Amended) The method of claim 23 further comprising [the] a step of regulating discontinuously the starting content of glucose in the perfusate by a two-point control process in which the starting content of glucose in the perfusate is changed by a predetermined adjustment value when there is a control deviation.

68. (Amended) A method for continuously determining [the] a glucose concentration in a body fluid with glucose-containing perfusate, the method comprising the steps of:

providing a microdialysis probe, a measurement cell, and a control device,

inserting the microdialysis probe into the body fluid,

passing the perfusate having a starting content of glucose through the microdialysis probe [in alternating successive transport and dialysis intervals] at different flow rates to obtain a dialysate,

transporting the dialysate to the measuring cell,

obtaining measurement signals that correlate with the glucose content of the dialysate in the measuring cell,

measuring the measurement signals that correlate with the glucose content of the dialysate,

adjusting the starting content of glucose in the perfusate to [the] a glucose content of the body fluid with the control device in accordance with a command variable corresponding with the glucose concentration of the body fluid and being derived from the measurement signals of the measuring cell, and

determining the glucose concentration in the body fluid by either using a momentary starting content of glucose in the perfusate as a measure for the glucose content of the body fluid or by determining the glucose content of the body fluid directly from the obtained measurement signals.

71. (Amended) The method of claim 68 further comprising the step of measuring the glucose content of the perfusate before [it] the perfusate is passed into the microdialysis probe.

73. (Amended) The method of claim 68 wherein the perfusate flows through the microdialysis probe during transport intervals and dialysis intervals, the flow rate during the transport intervals is [increased to such an extent] greater than the flow rate during the dialysis intervals and is such that the starting content of glucose in the perfusate during passage through the microdialysis probe remains essentially constant and that during the dialysis intervals the transport of the perfusate is interrupted or at least the flow rate is reduced to such an extent that the glucose concentration of the dialysate approximates the glucose content of the body fluid.

74. (Amended) The method of claim 73 wherein the command variable is determined from [the] a peak value of [the] a signal time course of the measurement signals during each transport interval.

75. (Amended) The method of claim 68 wherein the command variable is determined from [the] a peak value of [the] a signal time course of the measurement signals [during each transport interval].

76. (Amended) The method of claim 68 wherein the command variable is determined according to the glucose content c of the body fluid according to the relationship

$$c = \left[\frac{S_g}{S_g \cdot (1-b) + b \cdot S_0} - 1 \right] \cdot a \cdot c_0 + c_0$$

in which S_g denotes [the] a peak value of the measurement signal and S_0 denotes [the] a base line value of the signals measured during a transport interval of the perfusate passing through the microdialysis probe and c_0 is the momentary starting content of glucose in the perfusate and a, b are empirically determined correction factors compensating for diffusion and mixing and remaining recovery effects during the transport interval.

77. (Amended) The method of claim 68 wherein the command variable is determined by integration or differentiation of [the] a time course of the measurement signals.

78. (Amended) The method of claim 68 wherein the command variable is determined by comparing [the] an actual signal curve of the measurement signals with calibrated signal patterns deposited in a storage medium.

79. (Amended) The method of claim 68 further comprising [the] a step of regulating discontinuously the starting content of glucose in the perfusate by a two-point control process in which the starting content of glucose in the perfusate is changed by a predetermined adjustment value when there is a control deviation.